REMARKS

In replying to the examiners request for election, certain changes and modifications to the claims have been made. Claims 2, 3, 4, 6, 8, and 11-17 have been amended, claims 9 and 10 have been cancelled, and claims 18-23 have been added to more clearly identify the present invention.

The examiner has required applicant to elect under 35 USC §121 a single disclosed species for the parachute structure complexed to one therapeutic compound through a linker. The examiner has provided, however, no suggestion as to the individual inventions which are to be chosen from in a manner that permits a concrete non-trivial reply. On the surface, one can interpret that the examiner is telling applicant that the invention is not what has been described in the specification and claims.

As described in the specification, the specific compounds in each component are not the invention that has been discovered and claimed. If every combination of specific compounds, which fit the disclosure must be applied for individually, a prohibitive number of applications and fees would result, without gaining the protection of the invention as disclosed. The essence of the invention would disintegrate into merely "trees lost in a forest", when the forest is the invention as disclosed. The examiner has identified no concrete reason to justify changing the invention to a set of subspecies individual inventions. Alternatively, examiner's language is unclear and the following selections, which retain the basic nature of the invention, will be adequate to proceed, although they too remove aspects of the invention from further examination at this time.

There is need to be able to consistently destroy tumor cells. The reliable disruption of a cell's membrane is one of the best ways to guarantee that a cell is permanently destroyed. The present invention provides a complex comprising a "parachute" structure which consistently and reliably brings a therapeutic moiety capable of disrupting a cell membrane, into a well defined position relative to that cell's membrane for sufficient time to allow activation and reaction of the therapeutic moiety and the cell membrane.

The parachute structures of the present invention are defined as hydrophilic moieties having a defined action diameter, based on attaching at least two sugar moieties of saccharides, amino saccharides, oligosaccharides and amino-oligosaccharides onto a multifunctional

branching moiety having at least three attachment sites such as triazine trichloride or trimesinic acid chloride.[i.e. having at least one additional attachment site for binding to the therapeutic moiety or the spacer moiety.]

Therapeutic compound is claimed as a photosensitizer or a chemotherapeutic drug. In the specification these are described as moieties having an active portion and a carboxyl group for attachment to the branching unit of the parachute structure or to the spacer. Photosensitizers are identified as: porphyrins, pheophorbide, bacteriopheophorbides, chlorins, bacteriochlorins, and purpurins. Chemotherapeutic drugs are identified as membrane active drugs of which an example is Merphalene.

The "linker" referred to by the examiner does not match up with the invention as claimed, unless it is in reference to the spacer which is not a critical component of the inventive complex, but is contained in a group of preferred embodiments. Examples are described in claims 8 and 9. The selection of a specific molecule depends on the cell targeted, i.e. the demands on the placement of the therapeutic agent relative to the cell's membrane.

The classes of compounds/moieties for the two critical components of the invented complex as well as that of the preferred embodiment having a spacer component are spelled out in the specification and to some extent in the claims.

To comply with the requirements of 37 CFR § 1.143, strictly for simplifying searching, it is suggested that the parachute structure be based on sugar/aminosugar residues such as glucosamine bonded to a trifunctional branching unit such as triazine trichloride or trimesinic acid trichloride. For the preferred embodiment having a spacer, a poly-aminoacid, a beta-aminoacid or gamma-aminoacid would be the preferred class for this optional component of the complex. Therapeutic examples have been given above, as photosensitizers or membrane active drugs, such as Merphalene.

To provide the examiner with a clearer starting point for searching, a supplemental prior art search has been conducted. The most relevant art concerns the delivery of a biologically active substance across a cell wall through the use of a molecular complex. Copies of the patents are enclosed for the examiners convenience. Please note that Kondratyev is the only patent

found that could be considered "prior" art. All other patents were issued and published after the filing date of the present application.

U.S. Patent No. 5,502,037 to Kondratyev discloses pro-cytotoxic drug conjugates comprising a homing agent first moiety, a spacer molecule second moiety linked to the homing agent, and a third moiety covalently linked to the second moiety consisting of a cytotoxic drug. The drug is non-toxic extracellularly but after internalization is metabolized to a cytotoxic metabolic product which arrests cell growth.

U.S. Patent No. 6,287,857 to O'Riordan et al. discloses a nucleic acid delivery vehicle construct for transfecting or infecting a target cell. The construct is made of a delivery vehicle and a bifunctional complex for linking the delivery vehicle to a target cell. The bifunctional complex has a delivery vehicle-binding molecule, a molecule that bind binds to a cell surface molecule on the target cell and a linker that connects the molecules.

U.S. Patent No. 6,245,359 to Milstein et al, discloses methods for transporting a biologically active agent across a cellular membrane or a lipid bilayer. A complexing perturbant is used to reversibly transform a biologically active agent to form a transportable supramolecular complex. The perturbant contains at least one hydrophilic moiety and at least one hydrophobic moiety. The supramolecule comprises the perturbant non-covalently bound or complexed with the biologically active agent.

U.S. Patent No. 6,169,078 to Hughes et al. discloses materials and method for the intracellular delivery of substances. In a specific embodiment, substances are delivered into cells using a novel class of lipid compounds having a disulfide bond. The cationic lipid compound can be complexed with DNA for insertion into a cell, where the disulfide bond is cleaved to release the DNA.

U.S. Patent No. 6,300,3198 to Manoharan discloses an improved ingress of therapeutic and other moieties into cellular targets. Complexes are provided which carry therapeutic moieties to target cells. The complexes preferably feature cell surface receptor ligands to provide specificity. The ligands are preferably bound to the therapeutic moieties through polyfunctional manifold compounds

None of these prior art references discuss the use of molecular structures to externally anchor while internally localizing a therapeutic compound with respect to a cell wall/membrane. None of the prior art discloses the use of a complex having a parachute structure as a delivery and positioning device. The present invention is neither anticipated by nor made obvious in view of the prior art.

With these remarks it is believed that the requirements of 37 CFR and the MPEP have been answered and the disclosure and claims are now in condition for examination as one whole invention. Consideration is respectfully requested. An early and favorable response is earnestly solicited. Thank you.

Respectfully submitted,

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What is claimed is:

1. A complex for delivery and application of drugs to cell membranes or a defined distance from the membrane within cells comprising:

   at least one parachute structure; and

   at least one therapeutic compound.

2. (amended) A complex according to claim 1, wherein said parachute structure comprises hydrophilic moieties, and said hydrophilic moieties [are preferably sugar residues that] have a defined action diameter, and wherein said action diameter can be achieved by a branching unit to which said hydrophilic moieties are bound.
3. (amended) A complex according to claim 2, wherein said hydrophilic moieties are glucosamine molecules attach[ing]ed to said branching unit.
4. (amended) A complex according to claim 2, wherein said hydrophilic moieties [may be] are selected from a group consisting of monomers [or] and oligomers; [with] and where said hydrophilic moieties have specific attachment points to selectins on specific cells so that the complex is targeted to said specific cells.
5. A complex according to claim 1, wherein said therapeutic compound is a photosensitizer.
6. (amended) A complex according to claim 1, wherein said therapeutic compound is a chemotherapeutic drug.
7. A complex according to claim 1, wherein said parachute structure is directly bound to said therapeutic compound.
8. (amended) A complex according to claim 1, wherein said parachute structure is connected with said therapeutic compound by a spacer, and wherein [said spacer is preferably ß-aminoacids, γ-amino butyric acid, or poly-aminoacids, and wherein] type and number of said spacer used defines the distance of said therapeutic agent to cell membranes or its localization within the cell.
9. (Cancelled) [A complex according to claim 8, wherein said spacer is preferably an aliphatic, aromatic , or heterocyclic molecule,or an amino acid sequence.]
10. (Cancelled) [A complex according to claim 9, wherein said amino sequence has an enzyme cleavable breaking point.]

11. (amended) A complex according to claim 8, wherein using different numbers [or] and types of said spacer[s] to connect said therapeutic compound and said parachute structure delivers said complex into subcellular compartments at a defined distance from a surface of said subcellular compartments.
12. (amended) A complex according to claim 1, wherein said parachute structures are modified with signals for targeting said complex to a defined tissue[or]/cell type in an organism.
13. (amended) A complex according to claim [11]12, wherein said [modified] signals contain bridging structures like a Biotin-Avidin system.
14. (amended) A complex according to claim 1, wherein said complex can be used for destruction of cells, and wherein said cells are prokaryotic[, preferably bacteria].
15. (amended) A complex according to claim 1[4], wherein said complex can be used for destruction of cells, and wherein said cells are eukaryotic[, preferably human and animal cells].
16. (amended) A complex according to claim 5, wherein said photosensiti[s]zer is positioned close to said membrane during time of activation to render said photosensiti[s]zer more effective compared to a similar photosensiti[s]zer without said parachute structure.
17. (amended) A method for the selective destruction of eukaryotic[or]/prokaryotic cells comprising the steps of:
    a. administering a complex to a region wherein said complex contains at least one parachute structure and at least one photosensitizer; [and]
    b. waiting for a pretreatment time interval to allow said complex to selectively localize [at cell membranes or] at a defined position [within] with respect to a cell membrane; and
    c. irradiating [a] said region [where said complex was administered] for a defined treatment time interval and intensity to activate said photosensitizer [,]; wherein said treatment time interval and intensity are sufficient to achieve selective destruction of desired cells.

18. (added) A complex according to claim 2, wherein said hydrophilic moieties are sugar residues.

19. (added) A complex according to claim 8, wherein said spacer is selected from a group consisting of ß-aminoacids, γ-amino butyric acid and poly-aminoacids.
20. (added) A complex according to claim 19, wherein said spacer is selected from a group consisting of an aliphatic molecule, an aromatic molecule, a heterocyclic molecule, and an amino acid sequence.
21. (added) A complex according to claim 20, wherein said amino acid sequence has an enzyme cleavable breaking point.
22. (added) A complex according to claim 14, wherein said prokaryotic cells are bacteria.
23. (added) A complex according to claim 15, wherein eukaryotic cells are human/animal cells.